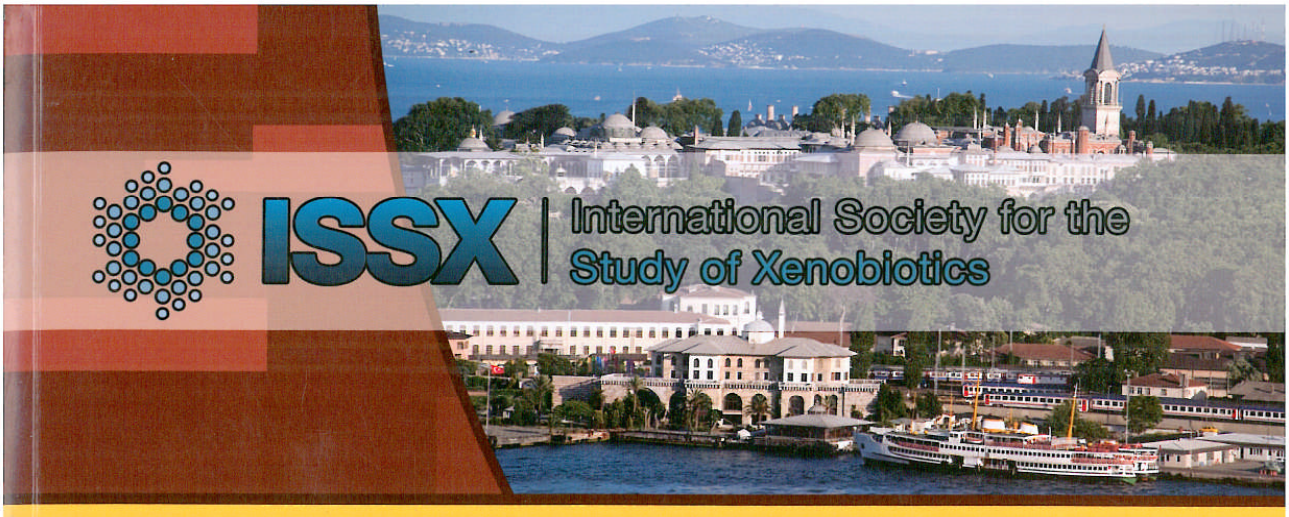

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PROGRAM & ABSTRACTS

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TÜBA

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P296. ACUTE DISRUPTION OF BONE MARROW HEMATOPOIETIC PROGENITOR CELLS BY BENZO(A)PYRENE (BP) IS REVERSED BY PROCESSES DEPENDENT ON AH RECEPTOR ACTIVATION

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We used colony forming unit (CFU) assays to demonstrate rapid suppression (within 6 h) of bone marrow (BM) lymphoid (CFU-preB) and myeloid (CFU-GM) progenitor cells in 7, 12-dimethylbenz(a)anthracene (DMBA) and benzo(a)pyrene (BP) treated C57BL/6 mice. The effects of BP are largely reversed with time (48-168 h), whereas those of DMBA increased. The duration of these changes were consistent with the blood levels of DMBA or BP and their metabolites following either IP or oral administration. BP and DMBA treatments both resulted in sustained BM toxicity in mice expressing a PAH-resistant Ah Receptor (AhR^d), suggesting that AhR activation is required to reverse the adverse effects of BP. Peripheral blood cell numbers were also reduced following DMBA or BP treatment. Reduction in blood cell numbers did not occur in Cyp1b1 null mice, indicating a requirement for extra-hepatic PAH bioactivation by Cyp1b1. Gene expression responses to DMBA showed constitutive activation of AhR linked genes in the BM adherent (stromal rich) cell fraction, whereas AhR linked genes needed to be induced by PAH treatment in the nonadherent cell fraction. BM adherent cell (stromal rich) gene responses to BP were more extensive than for DMBA, however AhR linked genes (Cyp1a1, Cyp1b1, AhRR, Spint1) responded equally to DMBA and BP. PAH treatment also altered expression of several developmental genes (Spint1, Ankra2, Egr1, Epha5, and Nfatc3) identified as novel AhR targets. These AhR linked responses were reversed in BP treated AhR^d mice, consistent with a requirement for AhR activation. BP treatment selectively increased gene expression of inflammatory factors (Cxcl2, Tnf, Cxcl10, Cox2 and IL1β) that are typically induced by oxidant-sensitive transcription factors. The absence of these inflammatory markers in AhR^d mice suggests that AhR activation by BP mediates pro-oxidant signaling, that in turn may be required for restoration of CFU progenitor cell functionality.

P297. ASSOCIATION OF BLOOD LEVEL OF METHEMOGLOBIN WITH CLINICAL OUTCOME OF PATIENTS WITH ALUMINIUM PHOSPHIDE POISONING

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Although methemoglobinemia following aluminum phosphide (AlP) intoxication has been reported, probable effect of blood level of methemoglobin (Met-Hb) on outcome of AlP intoxicated patients has not yet been investigated. This study aimed to evaluate this probable association. Methods: This prospective study was carried out at Loghman-Hakim poison hospital from April 2009 to August 2009 All patients aged >12 years who had ingested AlP and were admitted at the hospital were enrolled into the study. Using the co-oximetry, Met-Hb was measured at the time of admission and was repeated 24 hours later if the patient survived. Results: 48 AlP intoxicated cases including 24 males were enrolled into the study. Mean age of the patients was 25.5± 9.5 years. There was significant association between Met-Hb blood level which measured at the time of admission and mortality (2.4%± 7.1% in survivors versus 15.2%± 13.5% in non-survivors, P<0.001). The same association was found at the 2nd day of admission (2.9%±8.2% in survivors versus 26.5%±19.9% in non-survivors, P=0.02). Conclusions: The present study found an association between blood level of Met-Hb and mortality in AlP intoxicated cases. Whether prophylactic administration of vitamin C and methylene blue can improve outcome of AlP-intoxicated cases should be investigated in future investigations.

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P298. ATTENUATION OF NEUROTOXICITY INDUCED BY SUB-CHRONIC PARAQUAT ADMINISTRATION IN RATS BY DEPRENYL, QUERCETIN, GREEN TEA OR MALT EXTRACT

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The possible protective potentials of deprenyl (10 mg/kg, i.p.), quercetin (50 mg/kg, p.o.), green tea (1 mg/kg, p.o.) and malt extract (625 mg/kg, p.o.) against sub-chronic paraquat (PQ)-induced neurotoxicity in rats were examined. PQ was administered once weekly as a single injection (20 mg/kg, i.p.) with or without daily pretreatment with any of the chosen agents for 6 successive weeks. Survival rates and changes in total weight gain of animals were assessed.